Title: Full Board Review of Submitted Protocol

SOP Code: SOP 05-A/V5 dated 26th July 2017

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1. Purpose

The IEC should review and must approve, every research study involving human participants and other forms of studies, before the research is initiated. The IEC should evaluate the scientific rationale, scope and, methodology, and the ethical aspects of the study. The committee should evaluate the possible risks to the participants with proper justification as well as the expected benefits to participants/community. The adequacy of documentation for ensuring privacy & confidentiality should also be reviewed.

2. Scope

This SOP applies to the review of all protocols submitted for initial review and decisions thereof by the IEC

3. Responsibility

It is the responsibility of Member Secretary to identify the Primary Reviewer (PR) as per expertise and allocate the projects on e-EC software. All the IEC members can review all the protocols. However PR must review and give comments on e-EC software for the projects assigned to him/her by member secretary. PR, after reviewing each study protocol will lead the discussion on the relevant protocol in the subsequent meeting (refer to SOP 13).

4. Flow chart

No.	Activity	Responsibility
1	Determine the protocol for full board review.	Member Secretary
2	Selection and allocation of projects to IEC members on e-EC software	Member Secretary
3	Review of the assigned protocols on e-EC	IEC Member
4	Compile the comments of IEC members on e-EC software	Member Secretary

5. Detailed Instructions

5.1 Determine the protocol for full board review.

All research involving more than minimal risk, proposals/ protocols which do not qualify for exempted or expedited review and projects that involve vulnerable population and special groups shall be subjected to a full board review by all the members. While reviewing the proposals, the following situations may be considered as minimal risk and should be carefully assessed against the existing facilities at the research site for determining risk/benefit analysis.

a. Collection of blood samples by finger prick, heel prick, ear prick, or venipuncture:

I. From healthy adults and non-pregnant women who weigh normal for their age and not more than 500 ml blood is drawn in an 8 week period and frequency of collection is not more than 2 times per week;

II. From other adults and children, where the age, weight, and health of the participants, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected has been considered and not more than 50 ml or 3 ml per kg, whichever is lesser is drawn in an 8 week period and not more than 2 times per week;

III. From neonates depending on the haemodynamics, body weight of the baby and other purposes not more than 10% of blood is drawn within 48 – 72 hours. If more than this amount is to be drawn it becomes a risky condition requiring infusion/blood transfusion;

IV. Prospective collection of biological specimens for research purposes by noninvasive means. For instance:

1. Skin appendages like hair and nail clippings in a non-disfiguring manner;
2. Dental procedures - deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction of permanent teeth; supra and sub gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth;
3. Excreta and external secretions (including sweat);
4. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum or by applying a dilute citric solution to the tongue;
5. Placenta removed at delivery;
6. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
7. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
8. Sputum collected after saline mist nebulization and bronchial lavages.

b. Collection of data through non-invasive procedures routinely employed in clinical practice.
Where medical devices are employed, they must be cleared/approved for marketing, for instance -

I. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the participant or an invasion of the participant's privacy;

II. Weighing or testing sensory acuity;

III. Magnetic resonance imaging;

IV. Electrocardiography, echocardiography; electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow,

V. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

c. Research involving clinical materials (data, documents, records, or specimens) that will be collected solely for non-research (clinical) purposes.

d. Collection of data from voice, video, digital, or image recordings made for research purposes.

e. Research on individual or group characteristics or behavior not limited to research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

5.2 Selection and allocation of projects to IEC members on e-EC software (Selection of PR)

- The Member Secretary, IEC will assign PR based on expertise in the related field and experience along with nonscientific member to each research study for scientific, ethical and statistical review. The PR will be members of the IEC and will have to present a detailed relevant review of the assigned study.
- The Primary Reviewers will present the research study at a regular full board
- In case the PR is not in a position to review due to some reason, he/she should inform the Member Secretary, IEC at the earliest, so that the research study can be assigned to another member.
- In the event of his/her absence, a PR can send comments on the research protocols to the Member Secretary, which will be tabled and discussed during the meeting. However, a final decision on the research protocol will be arrived at, by a broad consensus at the end of discussion among attending members and not solely based on comments.
- It is the responsibility of the assigned PRs to review the research protocols assigned to them thoroughly and communicate their observations, comments and decisions to the IEC during the meeting. The PRs should return the research protocols and relevant documents to the secretariat on the day of the meeting.
- The Member Secretary can invite an independent consultant or expert (if necessary) for comments during the full board meeting.

5.3 Review of the assigned protocols on e-EC

- The protocol will be reviewed by each member as per guidelines (how to review a study protocol described in *AX 04/SOP 05-A/V5*.)
- The IEC member will consider the following criteria when performing the review of the study protocol:

➢ **5.3.1 Examine the qualification of investigators and assess adequacy of study sites**

The IEC members must consider whether the qualifications of the participating investigators relate to the study by reviewing their CVs, MMC Registration certificates and GCP training certificates (proceeding 3 years).

- The IEC members must examine disclosure or declaration of potential conflicts of interest
- The IEC members must assess / ascertain, if required by reviewing the study site whether the facilities and infrastructure at study sites can accommodate the study.

➢ **5.3.2 Scientific Design and Conduct of the Study**

- Is the project original and innovative? e.g. Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this area?
- Is this an attempt to validate, prove or disapprove the validity of existing knowledge?
- Appropriateness of study design, work plan and structure to achieve the stated objectives: Are the conceptual or clinical framework, design, methods and analyses adequately developed, well integrated, well reasoned and appropriate to the aims of the project?

- Relevance of the work in the context of contemporary translation or clinical cancer research:
  - ❖ Does this study address an important research question or is it a predominantly service proposal?
  - ❖ If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced?
  - ❖ What will be effect of these studies on the concepts, methods, technologies, treatments, services, or preventive interventions that drive this field?
- Appropriateness of the study design in relation to the objectives of the study;
- The statistical methodology (including sample size calculation), and the potential for reaching sound conclusions with the smallest number of research participants;
- The justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants and the concerned communities;
- The justification for the use of control arms;
- Potential of the work that would be conducted to lead into a larger and high impact study;
- Criteria for prematurely withdrawing research participants, and criteria for suspending or terminating the research as a whole;
- The adequacy of provisions made for monitoring and auditing the conduct of the research, including the constitution of a Data Safety Monitoring Board;
- Investigator's capability, availability of infrastructure and scientific environment to conduct the study within the time frame and carry it forward;
- The adequacy of the site, including the support staff, available facilities, and
- emergency procedures;
- Study Reporting and publication of the research.
- Regulatory permission for conduct of the study, HMSC clearance for international collaborative studies, MOU and CTA for national and international collaborative research.
  - ✓ minimize risks to participants;
  - ✓ risks must be reasonable in relation to anticipated benefits;
  - ✓ participants are selected equitably;
  - ✓ informed consent is adequate, easy to understand and properly documented;
  - ✓ the research plan makes adequate provision for monitoring the data collected to ensure the safety of participants, where appropriate;
  - ✓ there are adequate provisions to protect the privacy of participants and to maintain the confidentiality of data, where appropriate; and
  - ✓ Appropriate safeguards are included to protect vulnerable participants.

➢ **5.3.3 Review study participation**

The IEC member will examine for the presence of the following points while reviewing the patient information sheet/Informed Consent Form as per guidelines to review protocol and Informed Consent Document/Patient Information Sheet in *AX 04/SOP 05-A/V5.*

- Voluntary, non-coercive recruitment, participation/ withdrawal
- Procedures for obtaining informed consent

- Contents of the patient information sheet - title, objective, study design and procedures
- Contents and language of the informed consent document
- Translation of the informed consent document in the local languages
- Language used – plain and easy to understand by general public
- Contact persons with address and phone numbers for questions about research participants rights and study or injury
- Privacy and confidentiality
- Risks and discomforts – physical / mental / social
- Alternative treatments
- Benefits – to participants, community, institution and society
- Compensation for participation: (Whether it will act as undue inducement)
- Involvement of vulnerable participants
- Provisions for medical/ psychosocial support
- Treatment for study related injuries
- Compensation for study-related injuries: Reasonable
- Use of biological materials
- Check for provision for signatures with dates of participant, person conducting informed consent discussion, investigator and witness

➢ **5.3.4 Examine community involvement and impact**

The IEC members will also consider the following points in the protocol, Informed Consent Form/ Patient Information Sheet

- Community consultation
- Benefit to local communities
- Contribution to development of local capacity for research and treatment
- Availability of study results

5.4 Compile the comments of IEC members on e-EC software

The MS will compile the comments from each reviewer on e-EC software.

6. Glossary

Document	Document may be of any forms, e.g., paper, electronic mail (e-mail), faxes, audio or video tape, etc.
Pre-clinical study	Animal and *in vitro* studies provide information on possible toxicities and mechanisms of action, and starting doses for human studies.

Vulnerable research participants	A vulnerable category of research participants includes children, prisoners, pregnant women, handicapped or mentally disabled persons, refugees, displaced persons and economically or educationally disadvantaged persons, who are likely to be vulnerable to coercion or undue influence.
Initial Review	The first time review of that protocol made by two or three individual reviewers (IEC members or non-members) in advance of the full Committee meeting, and comments of the reviewers will be reported to the full Committee meeting.
Phase I studies	Initial introduction of an investigational new drug (IND) into humans, studies designed to determine the metabolism and pharmacological actions of drugs in humans, and studies designed to assess the side effects associated with increasing doses.
Phase II study	A Study of drug metabolism, structure-activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes.
Phase III study	A Study expands controlled and uncontrolled trials performed after preliminary evidence suggesting effectiveness of the drug has been obtained. They are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling.
Phase IV study	A study that seeks to expand an approved medication's use into a new population, new indication, or new dose.
Minimal Risk	It means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. However, in some cases like surgery, chemotherapy or radiation therapy, great risk would be inherent in the treatment itself, but this may be within the range of minimal risk for the research participant undergoing these interventions since it would be undertaken as part of current everyday life. Example for minimal risk: A retrospective review of patient case records to determine the incidence of disease/ recurrence of disease]
Less than minimal risk:	Research, in which there is no known physical, emotional, psychological, or economical risk to the study participants. This research qualifies as exempt if it does not involve special populations (i.e., minors, prisoners, pregnant women, etc.)

Benefit	A research benefit is considered to be something of a health-related, psychosocial, or other value to an individual research subject, or something that will contribute to the acquisition of generalizable knowledge. Money or other compensation for participating in research is not considered to be a benefit. A great deal of research in the social and behavioral sciences offers little potential for direct benefits to the subjects themselves. Rather, the benefits often encompass the importance of the knowledge to be gained, and/or to the contributions the research makes to science or society.

7. References

[1] World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000) - *www.who.int/tdr/publications/publications/* (last accessed 31st July 2017)

[2] International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996 - *http://www.ich.org/LOB/media/MEDIA482.pdf* (last accessed 31st July 2017).

[3] Cavazos N., Forster D., and Bowen A.J., Ethical Concerns in Placebo-controlled studies: An Analytical Approach, Drug Information Journal 36(2) 2002: pgs 249-259, via WIEC documents

[4] Assessment of risk and potential benefit. https://bioethicsarchive.georgetown.edu/nbac/capacity/Assessment.htm. (accessed on 31st July 2017)

[5] Bernabe et al.: The risk-benefit task of research ethics committees: An evaluation of current approaches and the need to incorporate decision studies methods. BMC Medical Ethics 2012 13:6.

8. Annexure

Annexure 1	*AX 01/SOP 05-A/V5*	IEC Decision Form
Annexure 2	*AX 02/SOP 05-A/V5*	Format of Project Approval letter (Interventional study)
Annexure 3	*AX 03/SOP 05-A/V5*	Format of Project Approval letter (observational study)
Annexure 4	*AX 04/SOP 05-A/V5*	Guidelines for reviewing a study protocol

Annexure 1

AX 01/SOP 05-A/V5

IEC Decision Form

Date of IEC meeting: _____

Protocol number: _____

IEC Protocol No. and Title:			
Principal Investigator:		Department:	
Final Decision at the meeting:	Approved		
	Minor modification	MS	
		MS + PR	
	Major modification	MS + PR	
		MS + PR+ FB	
	Disapproved (Reason)		
	Monitoring required (Reason)		

No.	Names of Members present	Approved	Modification		Disapproved	Signature
			Major	Minor		

Comments:

No. of members voting for the decision:

No. of members voting against the decision:

No. of members abstaining from voting:

_____

Signature of Chairperson **Date:** _____

Annexure 2

AX 02/SOP 05-A/V5

Format of Project Approval letter (Interventional study)

Date XX/XX/XXXX

To,

Dr. xxxxxxxxxxxx,

Dept. of xxxxxxxxxxxxx.

Ref:The project no. EC/xxx/20xx entitled, "xxxxxxxxxx".

Sub: Letter no.

Dear Dr. XXXXx,

The meeting of the Institutional Ethics Committee (IEC) was held on xxxxx at xxxx, in the xxxxxxxxxxxxx with xxxxx as Chairperson.

xxxx members attended the meeting held on xxxx. The list of members who attended the meeting is as follows.

Name of Members	Position on IEC	Designation & Affiliation	Qualification	Gender

It is hereby confirmed that neither you nor any of the study team members have participated in the voting/decision making procedures of the committee.

The IEC reviewed the above mentioned clinical study and approved the following documents submitted for this clinical study at the meeting.

1. Xxx
2. Xxx
3. xxx

The IEC hereby approves the proposal entitled, "xxxxxxxxxxxxx".

It is understood that the study will be conducted under your direction, in a total of xxxx research participants, at Dept. of xxxx, Seth G. S. Medical College and K. E. M. Hospital as per the submitted protocol.

This approval is valid for the entire duration of the study. IEC should be informed after the recruitment of first participant.

It is the policy of IEC that, it be informed about any onsite serious adverse event or the unexpected adverse event report within 24 hours as per the format specified in AX 01/SOP 14/V5 (Appendix XI of Schedule Y) and AX 02/SOP 14/V5 to the IEC or by email if there is holiday. The report of SAE or death after due analysis shall be forwarded by the Investigator to chairman of the IEC and the head of the institution where the trial is been conducted within 14 calendar days of SAE or death.

The sponsor has to forward the report of SAE or death after due analysis to the chairman of the IEC and the head of the institution where the trial is been conducted within ten calendar days of occurrence of the SAE or death. The report of the SAE other than death after due analysis shall be forwarded to chairman of the IEC and the head of the institution.

In case of injury or death occurring trial subject the sponsor (whether a pharmaceutical company or an institution) or his representative, whosever had obtained permission from the Licensing Authority for conduct of the clinical trial shall make payments for medical management of the subject and also provide financial compensation for the clinical trial related injury or death in the manner as prescribed in SOP 5 Annexure 6. (applicable for regulatory/interventional academic studies)

No deviations from, or changes of the protocol and Informed Consent Document should be initiated without prior written approval by the IEC of an appropriate amendment. The IEC expects that the investigator should promptly report to the IEC any deviations from, or changes of, the protocol to eliminate immediate hazards to the research participants and about any new information that may affect adversely the safety of the research participants or the conduct of the trial.

For studies which will continue for more than a year, a continuing review report needs to be submitted (within 1 month of the due date i.e. 11 months from the date of approval) on or before XXXXXXXXXXX.

A copy of the final report should be submitted to the IEC for review.

The IEC functions in accordance with ICH GCP, Schedule Y, ICMR guidelines and other applicable regulatory requirements.

Sincerely yours

Member Secretary,
IEC
(Signed and dated by the IEC Member Secretary)

Date of approval of the study: XX/XX/20XX

Annexure 3

AX 03/SOP 05-A/V5

Format of Project Approval letter (observational study)

Date XX/XX/XXXX

To,

Dr. xxxxxxxxxxxx,

Dept. of xxxxxxxxxxxxx.

Ref:The project no. EC/xxx/20xx entitled, "xxxxxxxxxx".

Sub: Letter no.

Dear Dr. XXXXx,

The meeting of the Institutional Ethics Committee (IEC) was held on xxxxx at xxxx, in the xxxxxxxxxxxxx with xxxxx as Chairperson.

xxxx members attended the meeting held on xxxx. The list of members who attended the meeting is as follows.

Name of Members	Position on IEC	Designation & Affiliation	Qualification	Gender

It is hereby confirmed that neither you nor any of the study team members have participated in the voting/decision making procedures of the committee.

The IEC reviewed the above mentioned clinical study and approved the following documents submitted for this clinical study at the meeting.

1. Xxx
2. Xxx
3. xxx

The IEC hereby approves the proposal entitled, "xxxxxxxxxxxxx".

It is understood that the study will be conducted under your direction, in a total of xxxx research participants, at Dept. of xxxx, Seth G. S. Medical College and K. E. M. Hospital as per the submitted protocol.

This approval is valid for the entire duration of the study.

No deviations from, or changes of the protocol and Informed Consent Document should be

initiated without prior written approval by the IEC of an appropriate amendment.

The IEC-II expects that the investigator should promptly report to the IEC any deviations from, or changes of, the protocol to eliminate immediate hazards to the trial subjects and about any new information that may affect adversely the safety of the subjects or the conduct of the trial.

For studies which will continue for more than a year, a continuing review report needs to be submitted (within 1 month of the due date i.e. 11 months from the date of approval) on or before xx xx xxxx.

A copy of the final report should be submitted to the IEC-I for review.

Sincerely yours,

Member Secretary,
IEC
(Signed and dated by the IEC Member Secretary)

Date of approval of the study: XX/XX/20XX

Annexure 4

AX 04/SOP 05-A/V5

Guidelines for reviewing a study protocol

Reviewers should think about and try to find answers to the following questions:

1. How will the knowledge, result or outcome of the study contribute to human well-being?
   - Knowledge from the basic research may possibly benefit.
   - A new choice of method, drug or device that benefits the research participants during the study and others in the future.
   - Provide safety data or more competitive choices.
2. Does the study design will be able to give answers to the objectives? Whether
   - The endpoints are appropriately selected.
   - The participating duration of a study participant is adequate to allow sufficient change in the endpoints.
   - The control arm is appropriately selected for best comparison.
   - The placebo is justified.
   - The number of study participants in non-treatment (or placebo) arm is minimized.
   - Unbiased assignment (e.g. randomization, etc.) is in practice.

- Inclusion and exclusion criteria are carefully selected to eliminate confounding factors as much as possible.
- The sample group size appropriate with the given statistical assumptions.
- Predictable risks are minimized.
- The tests and procedures that are more than minimal risk are cautiously used.
- Research participants deception is avoid.
- Instruction and counseling for study participants are included (if needed) when deception is integral to the study design.
- The study participants are adequately assessed and provided follow-up care, if needed.

3. Who will be the participants in the study? Whether
   - The described population is appropriate for the study.
   - Predictable vulnerabilities are considered.
   - It is completely necessary to conduct the study in a vulnerable population. If not, is there any other way to get the study answers?
   - There will be secondary participants.
4. Do the inclusion and exclusion criteria
   - Selectively include participants most likely to serve the objective of the study?
   - Equitably include participants?
   - Properly exclude participants who can predictably confound the results?
   - Properly exclude participants who may predictably be at increased risk in the study due to coexisting conditions or circumstances?
5. Does the study design have adequate built-in safeguards for risks?
   - Appropriate screening of potential participants?
   - Use of a stepwise dose escalation with analysis of the results before proceeding?
   - Does the frequency of visits and biological samplings reasonably monitor the expected effects?
   - Are there defined stopping (discontinuation) / withdrawal criteria for participants with worsening condition?
   - Is there minimized use of medication withdrawal and placebo whenever possible?
   - Will rescue medications and procedures be allowed when appropriate?
   - Is there a defined safety committee to perform interim assessments, when appropriate?
   - Is appropriate follow-up designed into the study? For instance, gene transfer research may require following the participants for years or for their entire lifetime after they receive the gene transfer agent.
6. Is pre-clinical and/or early clinical studies sufficiently performed before this study?
   - The animal study and *in vitro* testing results?

- Previous clinical results, if done?
- Whether the proposed study is appropriately built on the pre-clinical and/or early clinical results.
  - The selected dose based on adequate prior results?
  - Monitoring tests designed to detect expected possible risks and side effects?

7. Do the study and the informed consent process include issues of special concern, such as:
   - Waiver or alteration of consent?
   - Delayed consent (e.g., emergency treatment, etc.)?
   - Deception?
   - Sensitive information of participants that may require a confidentiality statement?
8. Risk benefits assessment categories:

Risk Categories

- The research involves less than minimal risk to subjects.
- The research involves minimal risk to subjects.
- The research involves more than minimal risk to subjects.

Benefits Categories

- The research provides no prospect of direct benefit to individual subjects, but likely will yield generalizable knowledge about subject's disorder or condition.
- The research provides no prospect of direct benefits to individual subjects, but likely will yield generalizable knowledge to further society's understanding of the disorder or condition under study.
- The research provides the prospect of direct benefits to individual subjects.
- The research provides no prospect of direct benefits to individual subjects, to science, or to society.

Guidelines to review Informed Consent Document/Patient Information Sheet

The actual process of informed consent should:

- Give the participants significant information about the study.
- Make sure the participants have enough time to carefully read and consider all options.
- Answer all questions of the participants before making decision to participate.
- Explain risks or concerns to the participants.
- Make sure that all information is understood and satisfied by the participants.
- Make sure the participants understand the study and the consent process.
- Obtain voluntary informed consent to participate.
- Make sure the participants can freely consent without coercion, pressure or other undue influences.

- Consent should be informally verified on a continuing basis.
- Continue to inform the participants throughout the study.
- Continue to re-affirm the consent to participate throughout the study.

Procedures or methods used in the informed consent process if recruitment of study participants include:

- A consent form
- Brochures, Pamphlets or other reading materials (i.e., letters to participants, phone pre-screening questionnaires, phone hold messages)
- Internet information
- Instruction sheets
- Audio-visual presentations
- Charts, diagrams or posters
- Discussions
- Consultation with others

Techniques to improve the readability of consent forms:

- Use short sentences and paragraphs
- Limit to one thought or topic in a sentence, avoid run-on sentence
- Use simple words, less syllables in a word.
- Use common words; remove technical jargon and medical terms.
- Try to use correct basic grammar and form.
- Use “gene transfer” instead of “gene therapy” (less implied effectiveness).
- Use “agent” instead of “drug” or “medicine” (less implied effectiveness).
- Try to avoid the use of “treatment”, “therapy” or “therapeutic” in studies involving gene transfer (because these words imply effectiveness)

Guidelines to Placebo Justification

Background conditions, such as benefits of standard treatment, risk of using placebo, risk management and disclosure should be considered. The followings are some guides to ease Board decision.

I. Benefits of standard treatment

1) Is there a standard treatment?
2) Is the standard treatment widely accepted?
3) Has efficacy of the treatment been consistently proven?
4) Are all newly diagnosed patients with this condition put in standard treatment (versus observed or other)?
5) Does the treatment act on the basic mechanism of the disease (vs. symptoms)?

6) Are most (≥85%) of the patients with this condition responsive to standard treatment alternatives (vs. resistant or refractory)?

If the answers of (1) to (6) are "yes", placebo is not recommended.

If any one or more answers are "no", placebo may be possible.

7) Are the side effects of the standard treatment severe?
8) Does standard treatment have many uncomfortable side effects?
9) Does standard treatment have contraindications that prevent some research participants from being treated?
10) Is there substantial (≤25%) placebo response in this disease or symptom?

If the answer of (7) *to* (10) *are "no", placebo is not recommended.*

If any one or more answers are "yes", placebo may be possible.

II. Risks of placebo

1) Is the risk of using placebo instead of treatment life threatening?

If yes, placebo is not acceptable.

2) Is the use of placebo instead of treatment likely to lead to permanent damage?

If yes, placebo is not acceptable.

3) Is the risk of using placebo instead of treatment likely to cause irreversible disease progression?

If yes, placebo is not acceptable.

4) Can the use of placebo instead of treatment lead to an acute emergency?
5) Is the risk of using placebo instead of treatment the persistence of distressing symptoms?
6) Is the risk of using placebo instead of treatment severe physical discomfort or pain?

If answers of (4) *to* (6) *are "yes", placebo is not acceptable unless risk management is adequate.*

III. Risk management

1) Is there benefit in the overall management of the research participants?

☐ *Yes, consider placebo*

☐ *No, placebo not recommended*.

2) Will the discontinuation of previous treatment put the participant in danger of acute relapse when transferred to placebo?

☐ *No, consider placebo*

☐ *Yes, placebo not recommended*.

3) Are research participants at high risk for the use of placebo excluded?

☐ *Yes, consider placebo*

☐ *No, placebo not recommended*.

4) Is the duration of the study the minimum necessary in relation to the action of the drug?

☐ *Yes, consider placebo*

☐ *No, placebo not recommended*.

5) Are there clearly defined stopping rules to withdraw the research participants in case he/she does not improve?

☐ *Yes, consider placebo*

☐ *No, placebo not recommended*.

6) Is risk monitoring adequate to identify progression of the disease before the research participants experience severe consequences?

☐ *Not applicable.*

☐ *Yes, consider placebo*

☐ *No, placebo not recommended*.

7) Are there clearly defined stopping rules to withdraw the research participants before the advent of severe disease progression?

☐ *Yes, consider placebo*

☐ *No, placebo not recommended*.

8) If the risk of placebo is an acute emergency, are rescue medication and emergency treatment available?

☐ *Not applicable.*

☐ *Yes, consider placebo*

☐ *No, placebo not recommended*.

9) If the risk of placebo is the persistence of distressing symptoms, is concurrent medication to control them allowed?

☐ *Not applicable.*

☐ *Yes, consider placebo.*

☐ *No, placebo not recommended*.

10) If the risk of placebo is severely physical discomfort or pain, is there rescue medication?

☐ *Not applicable.*

☐ *Yes, consider placebo.*

☐ *No, placebo not recommended*.

IV. Risk disclosure in the consent form

1) Are the risks of getting placebo instead of active treatment fully disclosed?

☐ *Yes, consider placebo.*

2) Are the risks of the test drug disclosed?

☐ *Yes, consider placebo.*

3) Are the advantages of alternative treatments explained?

☐ *Yes, consider placebo.*

Conclusions:

1. The use of placebo is ethically acceptable because:

☐ Research participants are not exposed to severe or permanent harm by the use of placebo.

☐ Research participants under placebo will benefit from the overall treatment of the disease.

☐ Risks of the use of placebo are minimized.

☐ Risks are adequately disclosed in the consent form.

Full Board Review

Initial Submission of Projects for full board Review

Submission of project proposal by Investigator [as per checklist – AX 02/SOP 05/V5]

For industry and Government sponsored studies submit Annexure 1-A (AX 01-A/SOP 05/V5) and for all academic (non sponsored) studies submit Annexure 1-B (AX 01-B/SOP 05/V5)

[Till 20th of every month eg. 20th June]

↓

Documents checked by the Administrative officer

Complete	Incomplete
↓	↓
Received by IEC	Returned
↓	
1st Review	

Review by the IEC members by circulation of projects [about 4 weeks] and Discussion at full board meeting 3rd/ 4th week of the next month.

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Decision communicated to investigator within 14 days of meeting (Approval/Disapproval with reasons/ Modifications in the proposal)

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Submission of response to IEC queries/modified project documents [to be submitted within 180 days after the IEC query letter is sent]

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2nd Review

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Member Secretary/ Chairperson, informed to members at full board meeting

two/more designated members, informed to members at full board meeting

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Full Board discussion

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Decision communicated to investigator within 14 days of meeting

(Approval/Disapproval with reasons/ Modifications in the proposal)